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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/854,816 | 05/15/2001 | Andrew C. Braisted | 9491-053-27 DIV | 1579 |

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| EXAMINER | |
|---|---|
| DELACROIX MUIRHEI, CYBILLE | |
| ART UNIT | PAPER NUMBER |
| 1614 | 12 |

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/854,816 | Applicant(s) BRAISTED ET AL. | |
|---|---|---|---|
| | Examiner Cybille Delacroix-Muirheid | Art Unit 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *1-3,6,7,10,13 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,8,9,11,12,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1A* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

***Detailed Action***

The following is responsive to Applicant's election received and Feb. 3, 2003.

Applicant's election of Group II, with a further election of species to the compound of Formula I, with traverse, is acknowledged. The traversal is on the grounds by requiring a further election of a consensus or homolog sequence, the Examiner has unduly limited the species, which would constitute a proper response. Furthermore, Applicant's assert that upon determination of allowability of the elected species of any of the generic claims, a subsequent examination of the additional species is required to determine the allowability of the whole of Applicant's invention.

Said arguments have been considered and are found to be persuasive. The request to elect a single consensus or homolog sequence is withdrawn. Next, as required, the Examiner will expand her search to the non-elected species, once a determination of allowability of the elected species is made. Finally, the Examiner respectfully maintains that the restriction requirement is proper not only for the reasons given previously in the action mailed Jan. 2, 2003 but also because each Group would raise different issues of patentability and would support separate patents. Please note that method claims 14-15 will be examined along with claim 8.

Claims 1-3, 6-7, 10, 13, 16 are withdrawn from consideration.

No prior art was found for the elected species, i.e. compound of Formula (I), so the search has been expanded to the non-elected species.

***Information Disclosure Statement***

Applicant's Information Disclosure Statement received Jul. 16, 2001 has been considered in part, i.e. US patents only. The remaining references are not in parent application 08/965,056. Applicant is respectfully requested to submit the references so that they may be considered and made of record. Please refer to Applicant's copy of the 1449 submitted herewith.

***Claim Objections***

1. Claims 8 and 14 are objected to because of the following informalities: in claim 8, the phrase "selected from the group...consisting of ...or.. is improper Markush terminology. The phrase should read –selected from the group...consisting of....and--. Please see MPEP 2173.05(h). In claim 14, line 2, after "administering" and before "a prophylactically or..", the phrase –to the mammal—should be added. Appropriate correction is required.

***Claim Rejections—35 USC 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 15 recites the limitation "the composition" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

5. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

**(1) The nature of the invention**:

The claims are drawn to constrained helical peptides and a method of using said peptides to prevent HIV infections in an individual.

**(2) The state of the prior art**

The obstacles to HIV therapy are well known. They include (1) the extensive genomic diversity and mutation rate associated with HIV retroviruses; (2) the fact that

the modes of transmission include both virus-infected mononuclear cells, which pass infecting virus to other cells in a covert manner, as well as via free virus transmission; (3) the existence of a latent form of the virus; (4) the ability of the virus to evade immune responses in central nervous system due to the blood brain barrier and (5) the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establishes that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed compounds to prevent HIV infection. The art further provides evidence of the difficulty in preventing HIV infections. Stein et al. (already of record in parent application 08/965,056) states that rational development to HIV therapeutics "is limited by our current knowledge of their mechanisms and effects and immune system's complex and overlapping activities" (see page 765, last paragraph). The reference to Fox (already of record in parent application 08/965,056), which describes the emergence of immune-system-boosting treatments in an attempt to treat HIV infections, concludes "no therapy has emerged as a sure winner in the campaign against HIV, not a preventive vaccine nor a therapeutic vaccine nor any of the immune-system-boosting treatments". See the Fox reference, last column, last full paragraph. Thus, it is clear from the art that the ability to prevent HIV infections is highly unpredictable and has met with little success.

**(3) The relative skill of those in the art**

The relative skill of those in the art is high.

**(4) The predictability or unpredictability of the art**

The unpredictability of the pharmaceutical and chemical art is high.

**(5) The breadth of the claims**

The claims are not very broad but, in addition to treatment, they require the prevention of HIV infection in a mammal.

**(6) The amount of direction or guidance presented**

Applicant's specification does not appear to provide guidance for the prevention HIV infection in mammals. The specification provides no guidance, to enable one of ordinary skill in the art to use the invention as claimed, which, as stated above requires absolute prevention of the infection. Furthermore, the specification appears to only be enabled for the inhibition of viral infection of cells in vitro using viral infectivity assays. It does not enable one of ordinary skill in the art to use the claimed invention in the complete prevention of HIV infection in mammals, i.e. in vivo. Applicant's specification does not set forth any examples of the claimed compounds, which would be capable of preventing HIV infection in a mammal.

**(7) The presence or absence of working examples**

There are no working examples, in vivo or in vitro, in the specification relating to the prevention of HIV. The only working examples in the specification involve the use of viral infectivity assays, which measure the inhibitory potency of the compounds in cells grown in vitro. Please see Example 4.

**(8) The quantity of experimentation necessary**

Since (1) it is clear from the art that the ability to prevent HIV infections is highly unpredictable and has met with little success, and (2) since the specification lacks guidance on how to use the claimed compounds in the actual prevention of HIV

infection, one of ordinary skill in the art would be burdened with undue experimentation to determine which of the claimed compounds and at what effective amount the compounds would be capable of completely preventing HIV infections in a mammal.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 4-5, 8, 9, 11-12, 14-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,271,198 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and USPN '198 claim constrained helical peptide compounds Formulae I, 6, 11 and 16 and methods of using the compounds to treat mammals infected with HIV.

The difference between the claims of the instant application and USPN '198 is that USPN '198 provides in claim 1 that Z is an amino acid sequence consisting of six amino acids with the described internal sequence. On the other hand claim 4 of the

instant application describes substituent "Z" as being "any amino acid consisting of six amino acids".

However, the scope of the claims of the instant application and the claims of USPN '198 overlap because claim 4 of the instant application is broader and encompass the claimed "subgeneric" compounds of USPN '198. Furthermore, the limitation concerning the six amino acids with the internal sequence as described for substituent "Z" in claim 1 of USPN '198 is found in dependent claim 8 of the instant application.

***Conclusion***

Claims 4-5, 8, 9, 11-12, 14-15 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Tue-Thur. from 8:30 to 6:00. The examiner can also be reached on alternate Mondays .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725 The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

Nov. 2, 2003

Cybille Delacroix-Muirheid
Patent Examiner Group 1600